Factors Affecting Surveillance Data on *Escherichia* coli O157 Infections Collected from FoodNet Sites, 1996–1999

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To determine the burden of illness caused by *Escherichia coli* O157 infections in populations in Foodborne Diseases Active Surveillance Network (FoodNet) surveillance areas, we initiated active, laboratory-based surveillance and surveyed laboratories, physicians, and the general public regarding the factors associated with the diagnosis and surveillance of infection with *E. coli* O157. We evaluated survey responses and site-specific incidence, outbreak, and demographic data during 1996–1999. A total of 1425 laboratory-confirmed cases of *E. coli* O157 infection and 32 outbreaks were reported from the 5 original FoodNet sites. The average annual incidence ranged from 0.5 cases/100,000 population in Georgia to 4.4 cases/100,000 population in Minnesota. After excluding outbreak-associated cases, the annual incidence of sporadic, laboratory-confirmed *E. coli* O157 infections remained relatively stable during 1996–1999, with a range of 1.9–2.3 cases/100,000 population. Regional differences in incidence partly resulted from differing physician and laboratory practices and from site-specific exposure factors (e.g., living on or visiting farms).

The Foodborne Diseases Active Surveillance Network (FoodNet) was developed to determine the burden and sources of specific foodborne diseases in selected states through active laboratory surveillance. A goal of FoodNet is to evaluate trends in the incidence of selected foodborne pathogens over time and to assess potential causes for changes in incidence. *Escherichia*

coli O157 is 1 of 7 bacterial pathogens under surveillance in FoodNet surveillance areas (also called "FoodNet sites"). *E. coli* O157 is a significant cause of diarrhea, bloody diarrhea, and hemolytic uremic syndrome, and it infects ~73,000 persons/year in the United States [1]. We summarized 4 years (1996–1999) of active surveillance data for *E. coli* O157 collected in FoodNet sites. Our goal was to document trends in the incidence and demographic characteristics of *E. coli* O157 infection by year and to identify potential reasons for site-specific differences in incidence.

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SUBJECTS AND METHODS

Study population. FoodNet is a collaborative effort involving the Centers for Disease Control and Prevention (CDC), the US Food and Drug Administration, the Food Safety and Inspection Service of the US De-

a Working group members are listed at the end of the text.

Table 1. Factors that affected the diagnosis of Escherichia coli 0157 infection in the original 5 FoodNet sites, 1996.

Factor	Site					
	California	Connecticut	Georgia	Minnesota	Oregon	
Unadjusted incidence of sporadic infection, cases/100,000 population	0.9	1.2	0.5	3.6	1.9	
Paitents with bloody diarrhea, a %	80	94	90	82	82	
Stool samples cultured in laboratories that cultured all bloody stool samples for <i>E. coli</i> O157, ^b %	69	96	58	90	92	
Physicians ordered a stool culture for the last patient they saw with bloody diarrhea, c %						
Yes	77	72	79	76	79	
No ^d	24	25	32	8	13	
Adjusted incidence of sporadic infection, cases/100,000 population	1.8	2.1	1.7	4.7	2.5	

^a From the 1997 FoodNet case-control study of sporadic O157 infections.

partment of Agriculture (USDA), and the CDC Emerging Infection Program [2]. Active, laboratory-based surveillance for E. coli O157 was initiated in 1996 in 5 FoodNet sites: Minnesota, Oregon, 2 counties in California, 2 counties in Connecticut, and 8 counties in Georgia. In 1997, surveillance was expanded to include a total of 3 counties in Connecticut and 20 in Georgia. By 1998, the areas under surveillance included the entire states of Connecticut, Minnesota, and Oregon and selected counties in California (2 counties), Georgia (20 counties), Maryland (6 counties), and New York (7 counties). By 1999, areas under surveillance included the entire states of Connecticut, Georgia, Minnesota, and Oregon and selected counties in California (2 counties), Maryland (6 counties), and New York (15 counties). Surveillance personnel at each site validated laboratory-confirmed cases of E. coli O157 infection by routinely contacting each clinical laboratory in their surveillance areas. We conducted the study in accordance with guidelines for human research as specified by the US Department of Health and Human Services.

Epidemiologic analysis. Surveillance data for laboratoryconfirmed infections were entered into the CDC Public Health Laboratory Information System and compiled at the CDC. The annual incidence for each site in cases per 100,000 population was calculated using the annual number of reported laboratoryconfirmed cases per site divided by the annual census estimates for the site. The number of sporadic E. coli O157 infections was calculated by subtracting the number of laboratory-confirmed, outbreak-associated cases from the total number of laboratory-confirmed cases observed in the FoodNet surveillance area. In this analysis, an outbreak was defined as ≥ 2 cases of laboratory-confirmed E. coli O157 infection in different households with an identified common source of exposure. Local or state health department personnel at each site did individual outbreak investigations.

An overall analysis of data from all FoodNet sites was done regardless of when the sites began active laboratory surveillance. To provide a consistent, longer-term picture of the incidence of *E. coli* O157 infection, a subset analysis of the original 5 FoodNet sites was done to document trends during 1996–1999. Data were analyzed using SAS software, version 6.12 (SAS).

Factors affecting a diagnosis of E. coli O157. To calculate the factors that affect the diagnosis of E. coli O157, data from previous FoodNet studies were used (table 1) [3–6]. Data included laboratory, physician, and population surveys and information from the 1996 FoodNet E. coli O157 case-control study [6].

For the FoodNet laboratory survey, during autumn 1995, all laboratories (n=230) that routinely tested stool specimens from residents of the original 5 FoodNet sites were identified and surveyed to determine laboratory culturing practices for *E. coli* O157 and the number of stool cultures performed during August 1995.

For the FoodNet physician survey, during January, April, July, and October 1996, a random sample of physicians (n=2939) in primary care and selected specialties in the original 5 FoodNet sites was surveyed to determine their practices with respect to culturing specimens obtained from patients with diarrhea [3]. To assess the effect of physician knowledge of laboratory practice on the reported incidence of E. coli O157, physicians were asked to name the primary laboratory where they sent stool specimens for bacterial culture and whether that laboratory always tested all stool samples for E. coli O157. Only physicians who submitted 100% of stool specimens to a single laboratory or to multiple laboratories that had the same practice were included in the analysis. We compared physician answers about laboratory practices for culturing E. coli O157 with the practices reported by the laboratories.

For the FoodNet population survey, during March 1996-

^b From the 1995 FoodNet laboratory survey.

^c From the 1996 FoodNet physician survey.

^d Because physicians thought the laboratory cultures all bloody stool samples for *E. coli* O157.

February 1997, a monthly random sample of households in each original FoodNet site was surveyed to determine the rate of diarrheal illness in the population and what proportion of persons with diarrhea sought medical care. Households were contacted by random-digit dialing by use of a sample design that increases calls in telephone bank strata with a higher probability of contacting a residential household.

For the FoodNet case-control study, during March 1996–April 1997, patients with laboratory-confirmed *E. coli* O157 infection were interviewed. Patients were asked whether they had experienced bloody diarrhea during the time they were infected. Data on 200 nonoutbreak cases and 380 age-matched control subjects were analyzed.

Calculation of adjusted sporadic incidence for original The incidence of sporadic, laboratory-con-FoodNet sites. firmed E. coli O157 infections for 1996 for each site was adjusted to account for site-specific laboratory, physician, and population practices using the following equation: $([A \times B]/[C \times D$ \times E]), where A is the unadjusted incidence of sporadic laboratory-confirmed E. coli O157 infections (by site; table 1, row 1), B is the percentage of patients in the FoodNet case-control study who had laboratory-confirmed E. coli O157 infection who reported bloody diarrhea (table 1, row 2), C is the percentage of stool samples that were cultured in laboratories from the FoodNet laboratory survey where all bloody stool samples are cultured for E. coli O157 (by site; e.g., 69% of stool samples cultured in California were cultured in laboratories that culture all bloody stool samples for E. coli O157) (table 1, row 3), D is the percentage of physicians from the FoodNet physician survey who ordered a stool culture for the last patient they saw who had bloody diarrhea (table 1, row 4), and E is 1 – the percentage of physicians by FoodNet site who did not request

E. coli O157 culture because they incorrectly assumed that their laboratory cultured all stool samples for *E. coli* O157, as determined from the FoodNet physician and laboratory surveys (table 1, row 5).

Estimation of the total number and incidence of sporadic E. coli O157 infection, by original FoodNet site. To estimate the incidence of total sporadic laboratory-confirmed cases of E. coli O157 infection by site, the adjusted sporadic rates were multiplied by disease-specific reciprocals. These reciprocals included the estimated sensitivity for culture of bloody diarrhea samples for E. coli O157 on sorbitol-MacConkey agar (71%), the percentage of persons with bloody diarrhea who reported in the population survey that they had visited their health-care provider (28%), and a percentage of all culture-confirmed E. coli O157 isolates from persons with bloody diarrhea who were identified from a series of cohort outbreak investigations (50%) [7–11]. Therefore, to calculate the estimated incidence of the total number of laboratory-confirmed and underreported cases of E. coli O157 infection by site, the site-specific adjusted incidence of laboratory-confirmed cases was divided by 0.0994 $(71\% \times 28\% \times 50\%)$. The site-specific adjusted incidence of laboratory-confirmed cases was divided by the estimated incidence of total culture-confirmed and underreported cases of E. coli O157 infection; this process was used to estimate the percentage of cases detected through laboratory surveillance.

RESULTS

All FoodNet sites. During 1996–1999, a total of 1734 laboratory-confirmed cases of *E. coli* O157 infection were identified in all FoodNet sites. Demographic and clinical data were reported annually during the 4-year period (table 2). The annual

Table 2. Demographic and clinical characteristics of patients with *Escherichia coli* 0157 infection in all FoodNet sites.

Variable	Data by year				
	1996	1997	1998	1999	
Total FoodNet population, in millions	14.3	16.1	20.7	25.6	
Total no. of patients	388	340	500	506	
Demographic					
Female, % of patients	54	52	51	53	
Aged <10 years, % of patients	44	48	48	41	
Clinical					
Hospitalized, % of patients	31	29	33	39	
With culture samples obtained Jun-Sep, % of patients	74	67	69	67	
Died, no. of patients	2	4	2	8	
With HUS, no. of patients ^a	26	11	20	34	
Incidence, cases/100,000 population	2.7	2.1	2.4	2.0	

^a Patients with hemolytic uremic syndrome (HUS) from whom *E. coli* O157 was isolated.

Table 3. Demographic and clinical characteristics of patients with *Escherichia coli* 0157 infection in the original 5 FoodNet sites.

Variable	Data by year				
	1996	1997	1998	1999	
Total FoodNet population, in millions	14.3	14.4	14.6	14.8	
Total no. of case patients	386	328	407	304	
Total no. of outbreaks (no. of outbreak case patients)	11 (104)	7 (56)	8 (78)	6 (25)	
Demographic					
Female, % of patients	54	53	51	50	
Aged <10 years, % of patients	44	47	50	36	
Clinical					
With cultures samples obtained Jun-Sep, % of patients	74	67	69	67	
Hospitalized, % of patients	30	29	31	37	
Died, no. of patients	2	4	2	3	
With HUS, a no. of patients	26	11	20	23	
Incidence, cases/100,000 population					
Observed	2.7	2.3	2.9	2.1	
Adjusted ^b	2.0	1.9	2.3	1.9	

^a Patients with hemolytic uremic syndrome (HUS) from whom *E. coli* O157 was isolated.

incidence in all sites combined ranged from 2.0 cases/100,000 population in 1999 to 2.7 cases/100,000 population in 1996. Some 911 cases (53%) occurred among female patients. Of case patients, 45% were aged <10 years (range, 41% in 1999 to 48% in 1997). Of case patients, 69% were identified during June–September (range, 67% in 1997 to 74% in 1996).

Of case patients, 564 (33%) were hospitalized (range, 29% in 1997 to 39% in 1999). There were 91 patients who received a diagnosis of hemolytic uremic syndrome (HUS), which accounted for 5% of laboratory-confirmed cases of *E. coli* O157 infection. The annual number of cases of HUS reported from all FoodNet sites was 11–34. Sixteen deaths were documented, for a case-fatality rate of 0.9%; each year, 2–8 deaths were attributed to *E. coli* O157 infection.

Original 5 FoodNet sites. During 1996–1999, there were 1425 laboratory-confirmed cases of *E. coli* O157 infection identified in the 5 original FoodNet sites. Similar demographic and epidemiologic findings (e.g., age and sex distribution, season of infection, and hospitalization rate) were observed between all FoodNet sites and the original 5 FoodNet sites (tables 2 and 3). The incidence of laboratory-confirmed *E. coli* O157 infection was 2.1 cases/100,000 population in 1999 and 2.9 cases/100,000 population in 1998 (table 3). Eighty cases of HUS were reported in the original 5 FoodNet sites, which accounted for 6% of the total number of culture-confirmed cases reported. Of laboratory-confirmed infections, 32% resulted in hospitalization; 11 cases (0.8%) were fatal.

Some annual variability was observed for the percentage of patients aged <10 years and the percentage of case patients who were hospitalized. During 1996–1998, the percentage of patients

aged <10 years increased from 44% to 50%, but the rate decreased significantly, by 1999, to 36% (P<.01, χ^2 = 15.1). During 1996–1999, the percentage of patients who were hospitalized was 29%–37%.

During 1996–1999, the average annual incidence of laboratory-confirmed infections varied markedly by site: by 0.5 cases/100,000 population in Georgia, by 1.2 in California, by 2.0 in Connecticut, by 2.4 in Oregon, and by 4.4 in Minnesota (figure 1). During the 4-year study period, the incidence in Georgia was 0.2–1.1 cases/100,000 population/year; the incidence in California was 0.9–1.6 cases/100,000 population, the incidence in Connecticut was 1.5–2.3, the incidence in Minnesota was 3.7–5.2, and the incidence in Oregon was 1.9–3.1.

Sporadic incidence in original FoodNet sites. A total of 263 laboratory-confirmed cases of E. coli O157 infection associated with 32 outbreaks were reported in the 5 original FoodNet sites. These 263 cases accounted for 18% of the 1425 reported laboratory-confirmed cases. Minnesota and Oregon reported 16 and 10 outbreaks, respectively. The fewest numbers of E. coli O157 outbreaks were reported in California (n=1), Connecticut (n=3), and Georgia (n=2). After excluding outbreak-associated cases, the average annual incidence for sporadic, laboratory-confirmed cases for the 5 original FoodNet sites combined was 1.9-2.3 cases/100,000 population (table 3). The incidence for sporadic, laboratory-confirmed cases was 2.0 cases/100,000 population in 1996 and 1.9 in 1999.

Factors affecting the diagnosis of E. coli O157. The following is an overview of results from the previous FoodNet studies used to calculate the factors that affect the diagnosis of E. coli O157 [3–6]. The percentage of patients with laboratory-

b Excludes outbreak-associated cases.

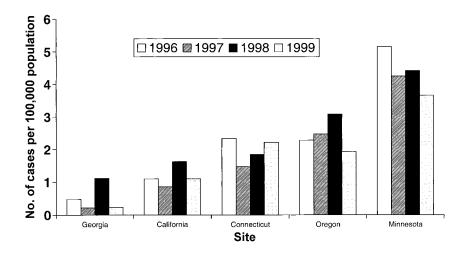


Figure 1. Incidence of laboratory-confirmed Escherichia coli 0157:H7 infections by FoodNet site, 1996–1999

confirmed *E. coli* O157 infection who reported having bloody diarrhea in the FoodNet case-control study was 80%–94% by site (table 1) [6]. The percentage of stool samples cultured for *E. coli* O157 in laboratories that cultured all bloody stool samples for *E. coli* O157 according to the laboratory survey varied markedly by site, from 58% of stool samples in Georgia to 96% of stool samples in Connecticut. Much less variability was noted in physician practices, with 72%–79% of physicians in the physician survey reporting that they had obtained a stool sample for culture from the last patient they saw who had bloody diarrhea. However, 8%–32% of physicians, by site, did not request a culture for *E. coli* O157 because they mistakenly thought their laboratory cultured all stool samples for *E. coli* O157.

These site-specific factors in the laboratory and physician surveys were used to adjust the sporadic incidence of laboratory-confirmed infections. In 1996, the unadjusted sporadic incidence of laboratory-confirmed cases ranged from 0.5 cases/ 100,000 population in Georgia to 3.6 in Minnesota, a 7-fold difference (table 1). The adjusted sporadic incidence of laboratory-confirmed cases in 1996 ranged from 1.7 cases/100,000 population in Georgia to 4.7 in Minnesota, an ~3-fold difference. These site-specific differences in laboratory and physician practices accounted for slightly more than one-half of the variability in incidence between sites.

To estimate the total number and incidence of sporadic *E. coli* O157 infections, the adjusted sporadic incidence of laboratory-confirmed cases was further adjusted by disease-specific factors. Adjusting for disease-specific reciprocals (the estimated sensitivity of *E. coli* O157 culture, the percentage of persons with bloody diarrhea who visited a health care provider, and the estimated percentage of patients with *E. coli* O157 infection who had bloody diarrhea), the estimated incidence of total sporadic *E. coli* O157 infections by site was 14 cases/100,000

population in Georgia, 18 cases/100,000 population in California, 21 cases/100,000 population in Connecticut, 25 cases/100,000 population in Oregon, and 48 cases/100,000 population in Minnesota. The incidence of total sporadic *E. coli* O157 infections by site was 13–34 times greater than the incidence of sporadic laboratory-confirmed *E. coli* O157 infections. Therefore, the estimated percentage of the total sporadic *E. coli* O157 infections that were laboratory confirmed and ascertained in the FoodNet surveillance sites was 3% in Georgia, 5% in California, 6% in Connecticut, 8% in Oregon, and 8% in Minnesota.

DISCUSSION

Several factors influence surveillance data. Differences in medical and laboratory practices, as well as in patient behavior (e.g., whether patients decide to seek medical attention for an illness), can have an effect on surveillance tallies, as do actual changes in disease incidence. Overall, the incidence of laboratory-confirmed E. coli O157 infections in FoodNet sites during 1996-1999 declined. This decline, however, was largely a result of variability in the occurrence of laboratory-confirmed E. coli O157 infections from outbreaks within the FoodNet sites during this period. When adjusting for outbreaks, the incidence of sporadic laboratory-confirmed E. coli O157 infections in the 5 original FoodNet sites remained stable. Large outbreaks and the enhanced case-finding efforts that often accompany them tend to overestimate the incidence in a given year. For example, in one day care center outbreak in Minnesota in 1996, there were 43 laboratory-confirmed cases of E. coli O157 infection identified; most of the laboratory-confirmed cases were identified through the systematic culturing of samples from all day care children and staff and likely would not have been identified had the outbreak not been investigated. If incidence estimates

are not adjusted for outbreaks, comparisons over a period of time and by region can be misleading. This is an important consideration, because 1996 was the first year of FoodNet data collection and represents a baseline against which incidences in subsequent years can be compared to evaluate the effect of prevention and control measures.

Although the aggregate incidence of sporadic, laboratoryconfirmed E. coli O157 infections in FoodNet remained stable, marked variability in incidence occurred between sites. The northern FoodNet states (i.e., Connecticut, Minnesota, and Oregon) consistently reported higher incidences; in addition, most of the outbreaks were reported in these states. In an earlier analysis, it was suggested that differing laboratory and physician practices in these sites appeared to account for 59% of this variability in sporadic laboratory-confirmed E. coli O157 infections [4]. In particular, the percentage of stool samples cultured in laboratories that routinely culture at least all bloody stool samples for E. coli O157 and physician knowledge of these laboratory practices appear to be important factors in the diagnosis of E. coli O157 infection [4, 5]. To facilitate identification, clinical laboratories are advised to test at least all bloody stool samples for E. coli O157 by culture on sorbitol-Mac-Conkey agar [12]. Furthermore, according to the results of a previous FoodNet study, many physicians incorrectly assumed that the clinical laboratories to which they submitted samples tested all stool samples for E. coli O157, which indicates a need for clearer communication between physicians and laboratory personnel [5]. Laboratories are encouraged to identify which organisms has been tested for when reporting negative bacterial stool culture results to physicians; similarly, physicians should check which organisms each laboratory tests for.

Physicians' practices concerning requests for stool cultures are dictated by a patient's presentation, history, and length of illness. In the FoodNet physician survey of randomly selected physicians, factors that promoted stool-culture requests included patients with bloody stools, a diagnosis of AIDS, diarrhea lasting >3 days, and recent travel to a developing country [3]. A similar study of physician practices at selected emergency departments found that physicians were more likely to request culture of stool samples from febrile patients or those who had visible blood in their stool [13]. Many factors may influence the ascertainment of cases of E. coli O157 infection, including the likelihood of that patient will seek medical attention, the proportion of patients for whom an appropriate laboratory test is requested, the ability of the testing process to confirm cases, and the appropriate reporting of cases [14]. It has been estimated that, for every reported case of laboratory-confirmed E. coli O157 infection, another 4-8 symptomatic cases are likely missed by current surveillance systems. We found that sitespecific rates of symptomatic cases per case reported were 13 in Minnesota and 34 in Georgia. However, these site-specific estimates must be interpreted with caution, because some physician and laboratory culturing practices, as well as the true incidence of *E. coli* O157 infection, can vary by year.

The variability in incidence rates between sites could also be explained by additional site-specific factors. Minnesota and Oregon had the highest average annual incidence of sporadic, laboratory-confirmed infection and accounted for 26 (81%) of 32 outbreaks in the 5 original FoodNet sites. Historically, investigations of E. coli O157 infection outbreaks have linked illness to the consumption of contaminated ground beef, lettuce, sprouts, apple cider, raw milk, jerky made from deer meat, and water; to direct contact with farm animals; and to personto-person transmission in day care settings [15-24]. Foods of bovine origin are commonly implicated as sources for E. coli O157 infection, and recent studies have documented a high prevalence of *E. coli* O157 in cattle [25, 26]. Serological evidence of E. coli O157 has been observed in 83% of range beef calves in Midwestern herds [27], and, in another study, E. coli O157 was found in the feces of 28% of cattle at slaughter in a Midwestern processing facility [28]. Preliminary results from the 1996 FoodNet E. coli O157 case-control study identified several risk factors associated with E. coli O157 infection [6]. These included the consumption of pink (i.e., undercooked) hamburger, the consumption of privately slaughtered ground beef or hamburger, and living on or visiting a farm. The consumption of privately slaughtered ground beef or hamburger and farm exposure reflects rural exposures more characteristic of the Minnesota and Oregon FoodNet sites. The 1997 USDA, National Agricultural Statistical Service, Census of Agriculture reported 2,400,000 and 1,600,000 cattle, respectively, in the Minnesota and Oregon surveillance areas [29]; only 8,200, 23,400, and 30,400 cattle were reported, respectively, from Connecticut, Georgia, and California counties under surveillance. Therefore, some of the observed differences in incidence of sporadic laboratory-confirmed E. coli O157 infections among the FoodNet sites may be associated with increased exposure to cattle (either directly or indirectly) in the sites with higher incidence. This ecological association between cattle populations and the site-specific incidence of E. coli O157 infection needs to be further characterized.

In summary, the incidence of sporadic, laboratory-confirmed *E. coli* O157 infection remained relatively stable during 1996–1999 among the 5 original FoodNet sites. A marked regional variability in incidence was observed among sites. The higher incidence in Minnesota and Oregon likely resulted from a combination of site-specific physician and laboratory practices and site-specific exposures associated with cattle. The public should continue to be educated about the health risks associated with the consumption of undercooked ground beef and hamburger, and meat processing facilities should be encouraged to use terminal pasteurization technologies (i.e., food irradiation) to

reduce end-product contamination. Other measures beyond current practices must be implemented to reduce the level of *E. coli* O157 infection in cattle and, ultimately, contamination in the processing facility. Also, as illustrated by the recent outbreaks of *E. coli* O157 infections associated with farm visits, additional efforts are needed to reduce transmission from farm animals to children [23]. A combination of these efforts will be necessary to reduce the incidence of *E. coli* O157 infection.

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